



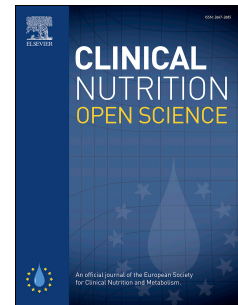
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Green tea consumption and SARS-CoV-2 infection among staff of a referral hospital in Japan

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Abstract

Background & Aim: This study examined the association between green tea consumption and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among Japanese.

Methods: Participants were staff of a large referral hospital in Tokyo. Green tea consumption was ascertained via a questionnaire. SARS-CoV-2 infection was identified through in-house records of PCR-confirmed COVID-19 cases or antibody tests. Multiple logistic regression was used to estimate the odds ratio of SARS-CoV-2 infection according to green tea consumption.

Results: Of 2640 participants (767 men and 1873 women; aged 21-75 years), 74 (2.8%) were confirmed or suspected to have been infected with SARS-CoV-2 during the epidemic.

Overall, SARS-CoV-2 infection was not significantly associated with green tea consumption.

There was a suggestion of a decrease in the odds of this infection associated with green tea consumption of ≥ 4 cups/day (odds ratio 0.51, 95% confidence interval 0.20–1.31).

Conclusions: Green tea consumption was not appreciably associated with the risk of SARS-CoV-2 infection. A lower odds of infection among those who consumed high green tea consumption deserves further investigation.

Keywords: coronavirus disease; green tea; Japanese; SARS-CoV-2

Introduction

The pandemic of coronavirus disease (COVID-19) has led to 241.9 million patients and 4.9 million deaths globally as of October 21, 2021 [1]. WHO has recommended infection prevention behaviors, including physical distancing and use of mask as well as vaccination [2]. Green tea has been suggested to lower the risk of influenza and upper respiratory tract infections [3]. Experimental studies show that epigallocatechin gallate, rich in green tea, inhibits infection and transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [4,5]. Countries with higher consumption of green tea are shown to have a lower morbidity/mortality rate of COVID-19 [6]. Here we examined the association of green tea consumption with COVID-19 infection in a cohort of healthcare workers in Japan.

Methods

The present study used data of ongoing repeat serological survey during the COVID-19 pandemic among workers of the National Center for Global Health and Medicine, Japan (NCGM) [7,8]. Participants were asked to donate venous blood and answer a questionnaire in each survey. We measured IgG (Abbott ARCHITECT®) and total antibodies (Roche Elecsys®) against the SARS-CoV-2 nucleocapsid (N) protein. Written informed consent was obtained from each participant. This study was approved by the ethics committee of NCGM. Green tea consumption was asked at the third survey, in which 2,779 participated (90%). Of these, we excluded those who lacked data necessary for the analysis, leaving 2640 aged 21-75 years (767 men and 1873 women) for analysis. We defined SARS-CoV-2 infection using two sources of information: the above-mentioned antibody tests (positive on either test at least once in the three surveys) and in-house records of PCR-confirmed COVID-19 cases. We asked about green tea consumption over the last month with six options ranging from “none or ≤ 2 day/week” to “ ≥ 4 cups/day” and divided participants into four (“ < 1 cup/day” to “ ≥ 4

cups/day”).

Baseline characteristics according to green tea consumption were expressed as mean (standard deviation) for continuous variables and percentage for categorical variables. Trend association between confounding factors and green tea consumption were tested using linear regression analysis for continuous variables, treating ordinal number in each category of green tea consumption as a continuous variable, and the Mantel-Haenszel chi-squared test for categorical variables. We run multiple logistic regression to estimate odds ratios of SARS-CoV-2 infection for green tea consumption with adjustment for age, sex, occupation, occupational risk of SARS-CoV-2 infection, infection prevention practice, body mass index (BMI), use of public transportation, high-risk behavior (2 items), and close contact with COVID-19 patient. Trend association was assessed by assigning ordinal numbers to the increasing category of green tea consumption and treating them as continuous. We repeated the analysis by information source (PCR-confirmed or antibody test positive only) and timing of infection (before or after vaccination of Pfizer-BioNTech). Additionally, we performed a sensitivity analysis using dichotomized category of green tea consumption (≤ 2 cups/day and ≥ 3 cups/day). Two-side P values < 0.05 were regarded as statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC. USA).

Results

Baseline characteristics of participants according to category of green tea consumption are shown in Table 1. Participants with higher consumption of green tea tended to have higher BMI and use public transportation (train or bus) compared to those with lower consumption. No other differences according to green tea consumption were observed.

Table 1

Characteristics of participants according to category of green tea consumption

	Green tea consumption (cup/day)				<i>P</i> for trend ^a
	<1	1-2	3	≥4	
No. of participants	1591	441	308	300	
Age (mean ± SD, years)	37.1 ± 11.5	41.7 ± 12.8	38.0 ± 12.9	37.3 ± 12.5	0.13
BMI (mean ± SD, kg/m ²)	21.7 ± 3.3	21.7 ± 3.1	21.8 ± 3.4	22.3 ± 3.6	0.006
Sex (men, %)	28.2	33.3	26.0	30.7	0.56
Occupation (doctor, %)	17.3	18.8	14.0	16.7	0.45
Risk of occupational exposure to SARS-CoV-2 (high, %)					
Infection prevention score ^b (mean ± SD)	5.7 ± 0.7	5.8 ± 0.5	5.7 ± 0.6	5.8 ± 0.6	0.17
Use of public transportation (train or bus) (≥5 d/wk, %)	40.0	47.8	43.2	49.7	0.001
Frequency of spending ≥ 30 minutes without mask in the 3C (none, %)	82.5	87.8	85.4	84.7	0.10
Frequency of having dinner with ≥5 people for ≥1 hour (none, %)	85.9	89.6	89.0	87.0	0.20
Close contact with a patient with COVID-19 (no, %)	89.1	89.1	87.0	87.7	0.29

Table 1 (continued)

^aBased on the Mantel-Haenszel chi-squared test for categorical variables and linear regression analysis for continuous variables, with ordinal number to category of green tea consumption.

^bInfection prevention score ranged from 0 to 6. Participants who reported “always” or “often” of the six items related to infection prevention measures (avoid 3Cs (crowded places, close-contact settings, and confined and enclosed spaces); social distancing; wear a mask when taking or when you are indoors; practice good cough etiquette; try not to touch eyes, nose, and mouth; wash or sanitize hands when you return home) received one point.

A total of 40 participants, including 19 who completed the second dose of vaccination, were identified through in-house records as having contracted with COVID-19. Of the remaining cases, 34 were positive on at least one SARS-CoV-2 antibody test. A total of 1049 (39.7%) drank green tea on a daily basis. Overall, there was no significant association between green tea consumption and SARS-CoV-2 infection (Table 2). However, there was a suggestion of decreased odds of SARS-CoV-2 infection associated with green tea consumption of ≥ 4 cups/day (multivariable-adjusted odds ratio 0.51, 95% confidence interval 0.20–1.31). The decreased, albeit not statistically significant, odds ratio associated with green tea consumption of ≥ 4 cups/day was observed for PCR-confirmed SARS-CoV-2 infection (multivariable-adjusted odds ratio 0.36, 95% confidence interval 0.08–1.58), antibody test-suggested SARS-CoV-2 infection (0.72, 0.21–2.44), COVID-19 diagnosed before vaccination (0.28, 0.04–2.24), and COVID-19 diagnosed after vaccination (0.46, 0.06–3.71).

Sensitivity analysis using dichotomized categories of green tea consumption showed similar results; the multivariable-adjusted odds ratios (95% confidence interval) of green tea consumption of ≥ 3 cups/day versus ≤ 2 cups/day were 0.62 (0.33–1.18) for SARS-CoV-2 infection, 0.64 (0.27–1.49) for SARS-CoV-2 infection confirmed with PCR, 0.60 (0.23–1.58) for antibody test-suggested SARS-CoV-2 infection, 0.44 (0.12–1.58) for COVID-19 diagnosed before vaccination, and 0.87 (0.28–2.68) for COVID-19 diagnosed after vaccination.

Table 2

Odds ratio (95% confidence intervals) of SARS-CoV-2 infection according to the category of green tea consumption.

	Green tea consumption (cup/day)				<i>P</i> for trend ^a
	<1	1-2	3	≥4	
PCR-confirmed or antibody test positive					
No. of cases/non-cases ^b	47/1544	15/426	7/301	5/295	
Age and sex-adjusted OR (95%CI) ^c	1.00 (reference)	1.25 (0.69–2.27)	0.78 (0.35–1.73)	0.55 (0.22–1.39)	0.23
Multivariable-adjusted OR (95% CI) ^d	1.00 (reference)	1.21 (0.66–2.22)	0.80 (0.35–1.81)	0.51 (0.20–1.31)	0.20
PCR-confirmed					
No. of cases/non-cases	24/1544	9/426	5/301	2/295	
Age and sex-adjusted OR (95%CI) ^c	1.00 (reference)	1.46 (0.67–3.18)	1.09 (0.41–2.88)	0.42 (0.10–1.78)	0.46
Multivariable-adjusted OR (95% CI) ^d	1.00 (reference)	1.33 (0.60–2.97)	1.04 (0.38–2.84)	0.36 (0.08–1.58)	0.34
Antibody test positive only					
No. of cases/non-cases	23/1544	6/426	2/301	3/295	
Age and sex-adjusted OR (95%CI) ^c	1.00 (reference)	1.02 (0.41–2.55)	0.45 (0.11–1.91)	0.69 (0.21–2.32)	0.33
Multivariable-adjusted OR (95% CI) ^d	1.00 (reference)	1.05 (0.42–2.66)	0.50 (0.12–2.15)	0.72 (0.21–2.44)	0.40

Table 2 (continued)

	Green tea consumption (cup/day)				<i>P</i> for trend
	<1	1-2	3	≥4	
PCR-confirmed before vaccination					
No. of cases/non-cases	14/1544	4/426	2/301	1/295	
Age and sex-adjusted OR (95%CI) ^c	1.00 (reference)	1.10 (0.36–3.40)	0.74 (0.17–3.30)	0.36 (0.05–2.76)	0.34
Multivariable-adjusted OR (95% CI) ^d	1.00 (reference)	1.01 (0.31–3.24)	0.62 (0.13–2.92)	0.28 (0.04–2.24)	0.20
PCR-confirmed after vaccination					
No. of cases/non-cases	10/1428	5/400	3/278	1/268	
Age and sex-adjusted OR (95%CI) ^c	1.00 (reference)	1.92 (0.65–5.71)	1.56 (0.43–5.72)	0.50 (0.06–3.96)	0.95
Multivariable-adjusted OR (95% CI) ^d	1.00 (reference)	1.79 (0.60–5.41)	1.67 (0.45–6.24)	0.46 (0.06–3.71)	0.92

Abbreviations: CI, confidence interval; OR, odds ratio; PCR, polymerase chain reaction.

Table 2 (continued)

^aBased on multiple logistic regression analysis with assignment of ordinal number to category of green tea consumption.

^bNegative PCR test and antibody test for COVID-19.

^cAdjusted for age (years) and sex.

^dAdditionally adjusted for occupation (doctors, nurses, co-medicals, clerical workers, or others), risk of occupational exposure to SARS-CoV-2 (low, middle, or high), infection prevention measures (avoid 3Cs (crowded places, close-contact settings, and confined and enclosed spaces); social distancing; wear a mask when taking or when you are indoors; practice good cough etiquette; try not to touch eyes, nose, and mouth; wash or sanitize hands when you return home), body mass index (kg/m^2), use of public transportation (train or bus) (<1 time/week, 1-2 times/week, 3-4 times/week, or ≥ 5 times/week), frequency of spending at least 30 minutes without mask in the 3Cs (none or ≥ 1 time), frequency of having dinner with five or more people for more than one hour (none or ≥ 1 time), and close contact with a patient with COVID-19 (no, yes, or unknown).

Discussion

In this study among healthcare workers in Japan, where green tea drinking is popular, there was no evidence of a significant association between green tea consumption and SARS-CoV-2 infection, which was confirmed by PCR or suggested by antibody tests. Nevertheless, people who consumed ≥ 4 cups/day of green tea had a lower, albeit statistically not significant, odds of SARS-CoV-2 infection, a finding compatible with experimental data showing that epigallocatechin gallate inhibits infection and transmission of SARS-CoV-2 [4,5].

The lower odds of infection associated with high green tea consumption was similarly observed across different outcomes (PCR-confirmed or antibody test positive only) and timings (infection before or after vaccination). This finding suggests green tea consumption prevents both symptomatic or asymptomatic infection, irrespectively of vaccination status. Experimental study shows that green tea can inhibit the infection of both wild-type SARS-CoV-2 and its variants with similar magnitude [4]. As the post-vaccination period of the present study corresponded to the epidemic of the Delta variant, the result may also give some support for the effect of green tea against the variant.

The present study was not large enough to detect the observed association with statistical significance. Large-scale investigations are required to confirm the present findings and to explore minimal consumption of green tea associated with lower risk of SARS-CoV-2 infection.

Conclusion

The present study did not find significant evidence to support a protective role of green tea consumption against SARS-CoV-2 infection among Japanese. A lower odds of infection among those with high consumption deserves further investigation.

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Declaration of competing interest

Abbott Japan and Roche Diagnostics provided reagents for anti-spike antibody assays.

Author contributions

TM and SY designed the research; NO supervised the research; SY, MK, and TM conducted the survey; AN performed statistical analysis; TM provided statistical expertise; AN drafted the manuscript; AN and TM had primary responsibility for the final content; and all authors approved the final version of the manuscript.

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